REMARKS

Favorable reconsideration of the instant application is respectfully requested in view of the above amendments and following remarks. Claims 1-11 are currently pending and under examination. By the present amendment, claims 1-3 are amended to more specifically recite particular aspects of the presently claimed invention. The above amendments are not to be construed as acquiescence to the stated grounds for objection/rejection and is made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application. Support for the amendments can be found in the claims as originally filed and in the specification, *e.g.*, on page 6, line 5.

Summary of Telephone Interview

Applicants wish to thank Examiner Tung for conducting a telephone interview with their representative, Dr. Carol D. Laherty, on March 2, 2007. During this interview, distinguishing features of the presently claimed methods as compared to the prior art references, Olek *et al.* and Herman *et al.*, were discussed and clarified. Specifically, the Examiner acknowledged that Herman *et al.* does not describe performing the deamination or desulfonation reactions while the nucleic acid is bound to a solid support and indicated that this basis of rejection would be withdrawn. In addition, the Examiner acknowledged that Olek *et al.* describe performing such reactions on nucleic acid that is "embedded" within the matrix of an agarose bead, as opposed to "bound" to agarose, and indicated that this basis of rejection would be withdrawn if this distinction is clearly made in the claims, *e.g.*, by adding a limitation to recite that the nucleic acid is "directly bound" to the solid support. In view of this telephone interview, it is Applicants' understanding that the present amendment and accompanying terminal disclaimer overcome all current bases of rejection.

Double Patenting

Claims 1-2 and 4-11 are provisionally rejected for alleged nonstatutory obviousness-type double patenting over claims 1-7 of Applicants' copending Application No.

10/540,406. Although the conflicting claims are not identical, the Examiner asserts that they are not patentably distinct from each other, because both claim sets are drawn to a method for conversion of a cytosine base to a uracil base, despite noting that Application No. 10/540,406 requires more specific temperature, bisulfite concentrations, and pH values for deaminating a nucleic acid.

Without acquiescence to any assertion made in the Action, Applicants submit herewith a Terminal Disclaimer with respect to Application No. 10/540,406 and respectfully request that the Examiner withdraw this basis of rejection.

Claim Rejections Under 35 U.S.C. § 102(b)

Claim 1 stands rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Olek *et al., Nucleic Acids Research*, 24(24):5064-66, 1996 (Olek *et al.*). In particular, the Action asserts that Olek discloses a reaction with nucleic acid embedded in an agarose gel, and that Olek *et al.* therefore "inherently" teaches that such nucleic acid is bound to a solid phase within the meaning of claim 1.

For reasons previously made of record and provided herein, Applicants traverse these grounds for rejection and submit that the claim 1 is novel in light of Olek *et al.* Claim 1 as amended herewith is directed to a method for the conversion of cytosine bases in a nucleic acid to uracil bases, comprising directly binding the nucleic acid to a solid phase. As described in the specification, directly binding indicates that the nucleic acid is directly bound without any compound mediating the binding to the solid phase (*see, e.g.,* page 6, lines 4-6 of the specification). Furthermore, the instant specification describes examples of techniques known to the skilled artisan that may be used to directly bind nucleic acids to a solid phase, including techniques that use chemical agents such as sodium iodide and sodium perchlorate (*see, e.g.,* page 7, lines 3-9).

Applicants respectfully submit that Olek *et al.* fails to teach a method wherein the nucleic acid is directly bound to a solid phase. In contrast, Olek *et al.* merely discloses reactions where the nucleic acid is "embedded," or "floating," in a low-melting temperature agarose matrix; the nucleic acid is not actually bound to the agarose matrix. Applicants note that while

the instant specification describes that the nucleic acid may be bound to the surface of pores within a solid phase, this is entirely different than being embedded within a matrix as described by Olek *et al.*

In support of this position, Applicants enclose a reference on agarose gel electrophoresis, which describes the use of an agarose *matrix* for separating nucleic acids based on size (*see,* Agarose Gel Electrophoresis - Wikipedia). In particular, this reference describes how negatively charged nucleic acid molecules *migrate through* a stationary agarose matrix towards an anode. Applicants submit that agarose-based electrophoretic separation of nucleic acids taught in this reference and well known to the skilled artisan would be impossible if the nucleic acids were in any way directly bound to the agarose matrix within the meaning of the instant claim.

In further support, Applicants enclose a reference describing the use of streptavidin agarose in the binding and chemical immobilization of nucleic acids (*see,* Kaboord *et al.*, *Biotinylated DNA binding capacities of Pierce avidin supports,* Pierce Biotechnology Inc. April 2006). Kaboord *et al.* describe the effective binding capacity of streptavidin-conjugated agarose for biotin-labeled nucleic acids. In particular, the purpose behind this reference suggests that nucleic acid do not bind to agarose beads in the absence of binding conjugates such as streptavidin/biotin. Rather, the use of strong, well-known binding conjugates on both the nucleic acid and the agarose is emphasized.

In view of the description of binding provided in the instant specification and the technical reasoning provided above, Applicants submit that the agarose in Olek *et al.*'s reaction does not bind directly to nucleic acid within the meaning of claim 1, and, therefore, Olek *et al.* contains no explicit or inherent teaching in this respect. Applicants note that in relying upon the theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990) (emphasis in original). Applicants submit that the Action has not made clear that "the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." (*Continental Can Co. USA v. Monsanto Co.,* 948

F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (M.P.E.P. § 2131.01 (III)). Indeed, as discussed above, it is clear that the nucleic acid described by Olek *et al.* is not, in fact, directly bound to the agarose. Accordingly, Applicants submit that Olek *et al.* fails to teach each element of the method of claim 1 and, thus, fails to anticipate the claimed subject matter. Applicants respectfully request that this basis of rejection be reconsidered and withdrawn.

Claims 2 and 3 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Herman *et al.* (U.S. Pat. No. 5,786,146). In particular, the Action asserts that Herman *et al.* disclose "binding the deaminated nucleic acid to a solid phase, eluting the deaminated nucleic acid from the solid phase, and incubating the deaminated nucleic acid under alkaline conditions," such that Herman *et al.* disclose all the limitations of the instant claims.

Applicants traverse these grounds for rejection and submit that the instant claims are novel in view of Herman *et al.*, since Herman *et al.* fail to disclose all the limitations of the instant claims. In particular, Herman *et al.* fail to perform or describe deamination or desulfonation reactions performed while the nucleic acid is bound to a solid support, as presently claimed. Claim 2 specifies that the sulfonation reaction is performed while the nucleic acid is bound to the solid phase (step d), and claim 3 specifies that the deamination reaction is performed while the nucleic acid is bound to the solid phase (step b).

In contrast, as conceded by the Action, Herman *et al.* perform deamination while the nucleic acid is in solution, subsequently purify the nucleic using a purification resin, and after eluting the nucleic acid from a solid phase, perform desulfonation while the nucleic acid is again in solution. Thus, all reactions occur while the nucleic acid is in solution and *unbound* to a solid phase support. In contrast, the instant claims require that either the deamination or desulfonation reaction takes place while the nucleic acid is *directly bound* to the solid phase. As such, the instant claims are clearly distinguishable from Herman *et al.* and Herman *et al.* fails to anticipate these claims. Accordingly, Applicants respectfully request that the Examiner withdraw this basis of rejection.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 4-11 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Olek *et al.* or Herman *et al.* as applied to claims 1-3, and further in view of Weindel *et al.* (WO 01/37291). In particular, the Action asserts that Weindel *et al.* disclose magnetic glass particles that can be used in nucleic acid purification, and that it would have been *prima facie* obviousness for one skilled in the art to apply the glass particles as a solid support for converting cytosine bases to uracil bases in a nucleic acid according to the instant claims.

For reasons previously made of record and discussed herein, Applicants traverse these grounds for rejection. Embodiments of the present invention as presently amended are directed in pertinent part to a method for the conversion of cytosine bases in a nucleic acid to uracil bases, comprising directly binding the nucleic acid to a solid phase, incubating the solid phase bound nucleic acid in the presence of sulfite ions whereby the nucleic acid is deaminated, incubating the solid phase bound deaminated nucleic acid under alkaline conditions whereby the deaminated nucleic acid is desulfonated, and optionally eluting the deaminated and desulfonated nucleic acid from the solid phase.

Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). In particular, the PTO must at a minimum show that the combined references teach or suggest all claim limitations. However, for reasons also given above in response to rejections under § 102, the claimed embodiments are readily distinguishable over both Olek *et al.* and Herman *et al.* which, alone or in combination, fail to teach or suggest (i) directly binding nucleic acids to a solid phase and (ii) performing deamination or desulfonation reactions while the nucleic acid is bound to the solid phase.

Moreover, as noted in the previous response, Weindel *et al.* does not remedy the deficiencies in either Olek *et al.* or Herman *et al.* In particular, Weindel *et al.* also fails to teach or in any way suggest directly binding nucleic acids to a solid phase and performing deamination or desulfonation reactions while the nucleic acid is bound to the solid phase.

Accordingly, none of the references cited by the Action, alone or in combination, teach all the elements of the claimed invention. Applicants therefore submit that the PTO has

failed to establish a *prima facie* case of obviousness, such that withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-11 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the Action asserts that the phrase "deaminated solid phase" is vague, and is therefore uncertain how the deaminated solid phase is made.

Applicants traverse these grounds for rejection and submit that the instant claims as presently amended are clear. Applicants note that the claims have been amended so that the terms "deaminated" and "desulfonated" are now directly before "nucleic acid" instead of "solid phase." Thus, it is clear that it is the nucleic acid and not the solid phase that is deaminated and desulfonated. Accordingly, the instant claims are directed in pertinent part to a method for the conversion of cytosine bases in a nucleic acid to uracil bases, comprising directly binding the nucleic acid to a solid phase, incubating the solid phase bound nucleic acid in the presence of sulfite ions whereby the nucleic acid is deaminated, yielding a solid phase bound deaminated nucleic acid, optionally washing the solid phase bound deaminated nucleic acid, incubating the solid phase bound deaminated nucleic acid under alkaline conditions whereby the deaminated nucleic acid is desulfonated, optionally washing the solid phase bound deaminated and desulfonated nucleic acid, and optionally eluting the deaminated and desulfonated nucleic acid from the solid phase.

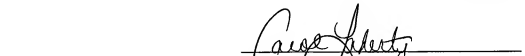
Applicants respectfully submit that the instant claims as amended are clear, and respectfully request withdrawal of the indefiniteness rejection under 35 U.S.C. § 112, second paragraph.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Favorable consideration and a Notice of Allowance are earnestly solicited. In view of the telephone interview conducted with the Examiner, Applicants believe that all of the claims remaining in the application are now allowable. However, should any issues remain, Applicants request that the Examiner contact the undersigned at (206) 622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Enclosures:

Terminal Disclaimer
Agarose Gel Electrophoresis - Wikipedia
Biotinylated DNA Binding Capacities of Pierce Avidin Supports

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